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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/647,457	11/29/2000	Meir Shinitzky	24390	6935

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EXAMINER	
TURNER, SHARON L	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 01/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/647,457	SHINITZKY ET AL.	
	Examiner	Art Unit	
	Sharon L. Turner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,7,8,11,13 and 14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,7,8,11,13 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1,3,7,8,11,13 and 14* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10-6-04 has been entered.

2. The amendment filed 8-6-04 has been entered into the record and has been fully considered.

3. The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

4. As a result of Applicant's amendment, all rejections not reiterated herein have been withdrawn by the Examiner.

5. Claims 1, 3, 7-8, 11, and 13-14 are pending.

Election/Restriction

6. Applicant's previous election with traverse of Group I, claims 1-6, 8, 10-11 and 13-14 in part to the extent drawn to the technical feature of SEQ ID NO:2 in Paper No. 10 (4-29-02) is acknowledged. The traversal is on the ground(s) that there is no appropriate explanation of serious burden. Applicants submit that there is no serious burden because a search of any one of the inventions would require searching areas appropriate to the other inventions and further because Applicants would be forced to pay further fees for search and examination of the additional inventions. This is not

found persuasive because as previously set forth the technical features differ in sequence structure, function, effects and are capable of distinct utilities. There is extensive search burden in examining all the inventions in a single application because the search for any one group is not co-extensive with a search for any other group, in particular the sequence searches are different for each invention. The fee structure has been determined by the Office to be appropriate compensation for the burden of search and examination of alternative inventions.

The requirement is still deemed proper and is therefore made FINAL.

7. It is noted for the record that original SEQ ID NO:2 is now SEQ ID NO:3 as amended by the new CRF and Sequence listing, see amendments of 9-16-03 and 1-9-04.

8. Newly amended claim 1 is directed to a new genus as defined in claim 1. The new sequence identifier of SEQ ID NO:1 and noted generic sequence of claim 1 as amended 8-6-04 now encompasses (is generic to) elected SEQ ID NO:3. However, the generic sequence is not apparently supported within the specification as originally filed or as amended in the CRF and paper copy of the sequence listing as submitted 9-16-03 and 1-9-04 as the definitions of Xaa residues as set forth in the paper copy of the sequence listing do not correspond to the definition denoted within the claim. Generic SEQ ID NO:1 is newly found to be unpatentable as anticipated by the prior art, see 102 rejections as below. Accordingly, the invention is non-linking to the alternative sequence identifiers and search has not been expanded over SEQ ID NO:1 and 3 as previously and instantly conducted.

Sequence Compliance

9. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth herein. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) before the application can be examined under 35 U.S.C. §§ 131 and 132.

In particular, claim 1 denotes particular limitations to the Xaa residues as in SEQ ID NO:1. However, these limitations are not in agreement with the notations within the computer readable format and paper copy of the sequence listing and accordingly the application is not in compliance with the sequence rules.

Correction of the computer readable format and paper copy of the sequence listing is required.

Claim Objections

10. Claims 3, 7-8, 11, 13-14 are objected to as being drawn to non-elected inventions, (as reciting an improper Markush Group and/or inventions that are non-linking). M.P.E.P. 803.02 states that:

"Since the decisions in In re Weber **,198 USPQ 328 (CCPA 1978); and In re Haas, 198 USPQ 334 (CCPA 1978), it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention, In re Harnish , 631 F.2d 716, 206 USPQ 300 (CCPA 1980); Ex Parte Hozumi , 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Broadly, unity of invention exists where compounds included within a Markush group (1) share a common utility and (2) share a substantial structural feature disclosed as being essential to that utility."

In particular it is noted that the additional sequences (SEQ IDNO's 2, 4-9) within claims 3 and 11 to which all claims are drawn lack unity and a common core structure and thus remain drawn to non-elected inventions. SEQ ID NO:1 is generic to SEQ ID

NO:3. However, the generic sequence is anticipated and noted to contain new matter as set forth herein. None of the other representative sequences is shared with elected SEQ ID NO:3.

11. Claims 7-8 and 13-14 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. As previously noted SEQ ID NO:1 is not apparently generic to elected SEQ ID NO:3. Moreover, the dependent claims do not apparently further limit claim 1

Specification

12. The amendments filed 9-16-03 and 1-9-04 are objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: Those changes that are newly drawn to a generic sequence represented as new SEQ ID NO:1 within the sequence listing. The sequence represented is not apparently supported by the specification as originally filed. SEQ ID NO:1 is not described within the specification as it is newly set forth in the sequence listing and does not correlate with the claims.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

> art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. Claims 1, 3, 7-8, 11 and 13-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Applicants present newly claimed generic SEQ ID NO:1 as set forth in claim 1 and the newly submitted sequence listing of 1-9-04. Applicants point to support for the amendments at pp. 3-5 of the specification and within the originally filed claims. However, support for the new recitations as generically recited are not found and moreover the limitations do not apparently correspond.. Accordingly the recitations constitute new matter absent evidence for support within the full scope from the specification as originally filed.

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 1, 3, 7, and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Hedges et al., PNAS 91:2621-24, 1994.

Hedges et al., teach a sequence of phosphopyruvate hydratase a.k.a. alpha-enolase of SEQ ID NO:1, see in particular Hedges et al., PNAS 91:2621-24, 1994, as indicated in the attached alignment with result I50026 Pir 78 database, residues LVVGLCTGQIKTGAPC fitting the formula comprising SEQ ID NO:1 and thus the peptide corresponds to the noted formula and inherently provides the properties noted pertaining to this sequence, i.e., it is capable of binding antibodies found in elevated levels in body fluids of schizophrenic patients and having a cyclic three dimensional structure consisting of hydrophobic core and positively charged extension. Claims 3 and 7 are deemed as comprising as it depends from claim 1 and does not further designate the peptides as consisting of i.e., closed language. Claim 14 is directed to a kit of the same peptide of claim 1. Patentability is distinguished via the peptide content. Thus, the reference teachings anticipate claims 1, 3, 7 and 14.

17. Claims 1, 3, 7, and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Byrjalsen et al., WO98/10291, 12 March 1998.

Byrjalsen et al., teach a sequence of phosphopyruvate hydratase a.k.a. alpha-enolase comprising SEQ ID NO:1, see in particular SEQ ID NO:9, as indicated in the below attached alignment LVVGLCTGQIKTGAPC fitting the formula comprising SEQ ID NO:1 and thus inherently provides the properties noted of the required sequence, i.e., capable of binding antibodies found in elevated levels in body fluids of schizophrenic patients and having a cyclic three dimensional structure consisting of hydrophobic core and positively charged extension. Claims 3 and 7 are deemed as comprising as it depends from claim 1 and does not further designate the peptides as consisting of i.e.,

closed language. Claim 14 is directed to a kit of the same peptide of claim 1. Patentability is distinguished via the peptide content. Thus, the reference teachings anticipate claims 1, 3, 7 and 14.

```
RESULT 17
AAW54357
ID   AAW54357 standard; protein; 433 AA.
XX
AC   AAW54357;
XX
DT   14-AUG-1998  (first entry)
XX
DE   Alpha Enolase.
XX
KW   Endometrium; hyperplasia; adenocarcinoma; proliferative phase;
KW   2D gel electrophoresis; detection.
XX
OS   Homo sapiens.
XX
PN   WO9810291-A1.
XX
PD   12-MAR-1998.
XX
PF   05-SEP-1997;   97WO-GB002394.
XX
PR   06-SEP-1996;   96GB-00018600.
PR   08-APR-1997;   97GB-00007132.
XX
PA   (CLIN-) CENT CLINICAL & BASIC RES.
XX
PI   Byrjalsen I,  Larsen P,  Fey SJ;
XX
DR   WPI; 1998-207057/18.
XX
PT   Biochemical markers of human endometrium - useful for, e.g. diagnosis of
PT   hyperplasia and adenocarcinoma.
XX
PS   Disclosure; Page 21; 77pp; English.
XX
CC   Proteins AAW54349-W54364 are examples of proteins produced in the
CC   endometrium during the hyperplasia, adenocarcinoma or proliferative phase
CC   of the endometrium. The presence and quantities of these proteins can be
CC   detected using 2D gel electrophoresis comparison of cell lysates. The
CC   proteins can be used as biochemical markers to detect the phase of the
CC   endometrium and can be measured in body fluids, obviating the need for
CC   endometrial biopsies
XX
SQ   Sequence 433 AA;

  Query Match             78.8%;  Score 67;  DB 2;  Length 433;
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  Best Local Similarity   81.2%;  Pred. No. 0.0029;
  Matches   13;  Conservative    0;  Mismatches    3;  Indels    0;  Gaps
0;

Qy          12 LVVGLCTXQIKTGXXC 27
               ||||||| |||||  |
Db         383 LVVGLCTGQIKTGAPC 398
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18. Claims 1, 3, 7, 8, 11 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Taylor et al., Experimental and Molecular Pathology, (1985 Apri) 42(2)271-7 as further evidenced via McAleese et al., Eur. J. Biochem., 178:413-41, 1988, see in particular Figure 1 peptide sequence comprising SEQ ID NO:1 "SGETEDTFIADLVVGLCTGQIKTGAPCR".

Taylor teaches cytopathogenic cerebrospinal fluid from neurological and psychiatric patients. In particular, cerebrospinal fluids (CSFs) (samples containing platelet associated antibodies shed from platelets) were examined for the presence of a cytopathogenic component by an in vitro radioimmunoassay, see in particular Methods, pp. 271-2. No abnormal proteins were detected in CSF which produced cytopathic effects. The cytopathic effect was associated with high-molecular-weight material which was resistant to enzyme treatment. The effect persisted after extensive ultraviolet irradiation. The presence of the cytopathic effect was associated with increased CSF enolase levels. Accordingly detection of enolase antigen is recognized as associated with cytopathogenic CSF in schizophrenic patients as compared to controls. Claims 3 and 7 are deemed as comprising as it depends from claim 1 and does not further designate the peptides as consisting of i.e., closed language. Claim 14 is directed to a kit of the same peptide of claim 1. Patentability is distinguished via the peptide content. With respect to claim 8, the references denotes distinction or diagnosis amongst

schizophrenics with antibody radioimmunoassay distinguishing enolase antigen antibody interaction and notation of increased levels in schizophrenics. As claim 11 depends from claim 8 but does not distinguish the peptides via closed language the claim is interpreted as comprising. Thus, the reference teachings anticipate claims 1, 3, 7, 8 and 14.

Thus, the reference teachings anticipate the claimed invention.

19. Claims 1, 3, 7, 8, 11 and 13-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Neural tissue hypersensitivity in psychiatric disorders with immunologic features, Jankovic B D, Journal of immunology (1985 Aug) 135 (2 Suppl) 853s-857s as further evidenced via McAleese et al., Eur. J. Biochem., 178:413-41, 1988, see in particular Figure 1 enolase peptide sequence comprising SEQ ID NO:1 "SGETEDTFIADLVVGLCTGQIKTGAPCR".

Jankovic teach a study wherein, "the study population consisted of 1010 in patients (referring to patients suffering from neurological disease including schizophrenia) and 81 control subjects. Patients suffering from schizophrenia, cerebral atrophy of unknown origin, dementia, depression, mental retardation, and ethanol-induced brain deterioration (alcoholics) were skin tested with 25 micrograms of S-100 protein and neuron-specific enolase isolated from fresh human brain. Evaluation of delayed skin hypersensitivity reactions at 24 hr revealed a high incidence of positive responses to S-100 protein: heavy alcoholism, 96.8%; depression, 94.1%; cerebral atrophy, 92.6%; dementia, 91.2%; schizophrenia, 87.7%; and mental retardation, 69.4%. The incidence of positive reactions to neuron-specific enolase in schizophrenics

was 91.6%. Of 58 control subjects tested with S-100 protein, 6.8% were positive, whereas of 23 normal individuals tested with neuron-specific enolase, 6.4% developed mild skin reactions. These data suggest a close relationship between delayed hypersensitivity to neural tissue antigens and immunopsychiatric diseases, and they imply that cell-mediated immune mechanisms are involved in the pathogenesis of certain mental disorders." As in Table II, NSE is found in greater positivity in delayed type hypersensitivity response upon NSE peptide exposure in schizophrenics as compared to normal controls, 6.4%. As the DTH hypersensitivity test is in vitro the contacting is inclusive of using whole blood sample from patients. The level of binding of the noted samples is in the skin locale of injection of peptide and is accordingly isolated in location. Thus, the reference teachings anticipate the claimed invention.

Status of Claims

20. No claims are allowed.

Allowable Subject Matter

21. Peptides consisting of or comprising SEQ ID NO:3 are free of the prior art of record, as previously noted. Claims directed to such subject matter would be allowable if so presented.

Conclusion

22. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should

applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (571) 272-0894. The examiner can normally be reached on Monday-Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached at (571) 272-0961.

SHARON L. TURNER, PH.D.
PATENT EXAMINER

Sharon L. Turner, Ph.D.
January 21, 2005